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Long term remission with Sirolimus for a pediatric patient with an EBV-associated smooth muscle tumor after bone marrow transplantation

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Introduction

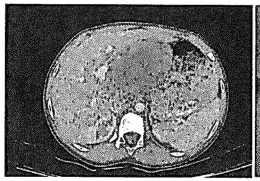
- Epstein-Barr virus (EBV) is a ubiquitous human herpes virus associated with a broad range of malignancies due to its oncogenic potential.
- Immunocompromised patients, especially those after transplantation have a strong disposition to EBV infection and development of smooth muscle tumors (SMTs)
- Lee et all described two cases in 1995 and discovered the link between EBV and the development of SMTs
- EBV-associated smooth muscle tumors (EBV-SMT) are rare with an estimated incidence of 1%-5%
- The incidence of EBV-SMTs after hematopoietic stem cell transplantation is extremely rare and reported only in a few cases with the majority occurring in pediatric patients
- Clear risk factors have not been identified including the type of immunosuppressive drugs, solid versus hematopoietic transplant, or manifestations of PTLD.
- Approximately 38% of transplant associated EBV-SMT and 40% of HIV-associated EBV-SMTs occur in children, and those related to immunodeficiency are rare and described in a few case reports

Case Presentation

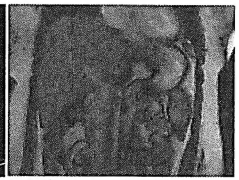
- A nine-year old female presented with acute onset abdominal pain, diarrhea, nausea, and vomiting.
- During her initial evaluations a CT scan of the abdomen and pelvis was obtained that showed numerous large heterogeneous masses in the liver
- Past medical history:
  - B-cell acute lymphoblastic leukemia (ALL)
  - Three years after treatment she had a relapse of her B-cell ALL and was treated with a matched allogenic bone marrow transplantation using male umbilical cord stem cells and achieved complete remission
  - Treated with immunosuppressive regimen including Tacrolimus, Mycophenolate, and Prednisone.
- Biopsy revealed a mesenchymal neoplasm with myofibroblastic proliferation consistent with a smooth muscle tumor .

Clinical Course

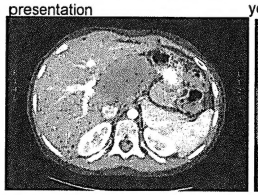
- A panel of markers including CD3, CD20, kappa, and lambda was performed and was negative, excluding the possibility of post-transplant lymphoproliferative disease.
- Tissue involvement with EBV was demonstrated by PCR and immunostaining for LMP-1 confirming the diagnosis of an EBV-SMT.
- She was started on Sirolimus, 1 mg, Prednisone, and antiviral therapy.
- Due to the size and multitude of masses in the liver surgical resection was not pursued.
- Repeat CT scan of the abdomen 12 months after initiation of therapy with Sirolimus showed decreased size of the liver masses .
- At her current evaluation, she remains without tumor progression and stable without relapse.



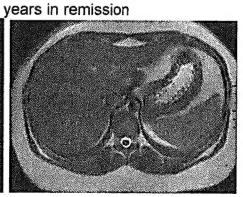
A. CT Scan at of EBV SMT at presentation



C. CT Scan at of EBV SMT 10 years in remission

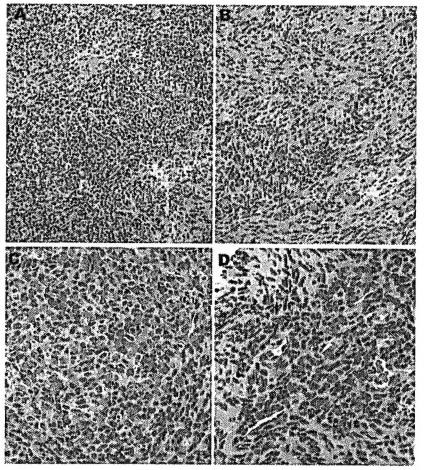


B. CT Scan at of EBV SMT at presentation



A. CT Scan at of EBV SMT10 years in remission

Pathology



- Figure 2: EBV-associated smooth muscle tumors morphologically resemble other smooth muscle tumors, being composed predominately of hyperchromatic spindled cells predominately in RNA.

Discussion

- This case represents the one of the few reported pediatric cases of long-term therapeutic responses with Sirolimus for EBV-SMTs.
- Due to the low incidence and varied clinical presentation of EBV-SMTs, knowledge of effective therapies are limited.
- Current treatment strategies include surgical resection, alterations in immunosuppression, anti-viral medications, and chemotherapy.
- AKT pathway and the mammalian target of rapamycin (mTOR) pathway are the most notable EBV pathogenesis pathways
- The mTOR pathway performs a key role smooth muscle proliferation and activation of the AKT/mTOR signal pathways via nuclear staining was observed in majority of tumors in several case reports
- Several case reports have demonstrated remission with Sirolimus, an mTOR pathway inhibitor, in patients with EBV-SMTs.
- Research on clinical improvement and remission for pediatric patients with EBV-SMT is limited and this case report demonstrates the long-term remission and therapeutic implications of early detection and initiation of therapy with Sirolimus for EBV-SMTs.

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